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Enantioselective Synthesis of Possible Diastereomers of Heptadeca-1-ene-4,6-diyne-3,8,9,10-tetrol; Putative Structure of a Conjugated Diyne Natural Product Isolated from *Hydrocotyle leucocephala*

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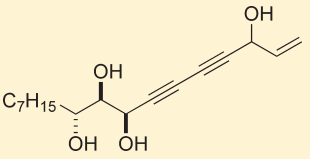
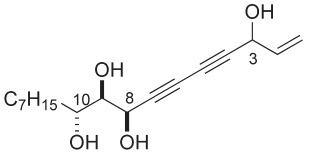
Supporting Information

ABSTRACT: Enantioselective synthesis of possible diastereomers of heptadeca-1-ene-4,6-diyne-3,8,9,10-tetrol, a structure proposed for the natural product isolated from *Hydrocotyle leucocephala* is accomplished. The reported spectral data of the natural product did not match those of any of the isomers that were synthesized and established that the structure proposed for the natural product is not correct and requires revision.



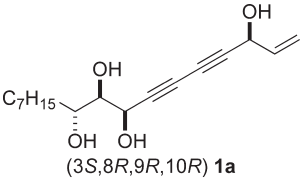
INTRODUCTION

Conjugated diyne containing natural products are an important class of compounds possessing diverse biological activities. With the isolation of conjugated diynes such as panaxytriol, which was found to exhibit inhibitory activity against MK-1 cells and to mitigate the growth of B16 melanoma cells, there has been a surge of interest in the synthesis of conjugated diynes and their analogues and derivatives with the aim of drug development.[1] Recently, Ramos et al. described the isolation of a conjugated diyne tetrol **1**, from the methanolic extract of *Hydrocotyle leucocephala*, an aquatic plant native of Brazil.[2] Structure of the diyne tetrol was proposed to be heptadeca-1-ene-4,6-diyne-3,8,9,10-tetrol **1**. Relative stereochemistry of the contiguous triol unit was assigned to be [8*R*,9*R*,10*R*] based on the method proposed by Kishi's group[3] for structurally related alkane triols; however, the stereochemistry at the C3 carbon was not assigned.

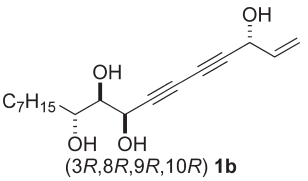


heptadeca-1-ene-4,6-diyne-3,8,9,10-tetrol **1**

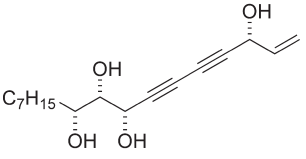
Recently, Ghosh and Pradhan disclosed the synthesis of both 3*R* and 3*S* isomers of the putative structure [8*R*,9*R*,10*R*] and found that the spectral data did not match with the published data of the natural product.[4] It was suggested that the natural product could be one of the other six diastereomers. In an effort to establish the relative as well as absolute structure of the natural product, we undertook the synthesis of the remaining six possible isomers **1c**−**h** of heptadeca-1-ene-4,6-diyne-3,8,9,10-tetrol, and we delineate our investigations in this article.



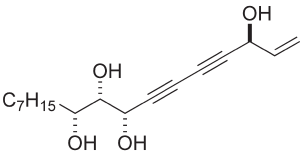
(3*S*,8*R*,9*R*,10*R*) **1a**



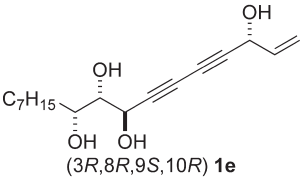
(3*R*,8*R*,9*R*,10*R*) **1b**



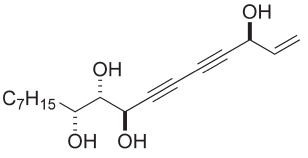
(3*R*,8*S*,9*S*,10*R*) **1c**



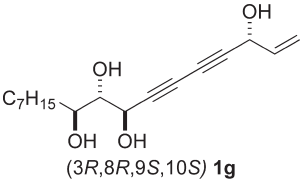
(3*S*,8*S*,9*S*,10*R*) **1d**



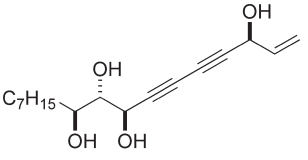
(3*R*,8*R*,9*S*,10*R*) **1e**



(3*S*,8*R*,9*S*,10*R*) **1f**



(3*R*,8*R*,9*S*,10*S*) **1g**



(3*S*,8*R*,9*S*,10*S*) **1h**

RESULTS AND DISCUSSION

At the outset, we focused on the synthesis of [3*R*,8*S*,9*S*,10*R*]-heptadeca-1-ene-4,6-diyne-tetrol **1c** and [3*S*,8*S*,9*S*,10*R*] heptadeca-1-ene-4,6-diyne-tetrol **1d** (Scheme 1). Synthesis of the

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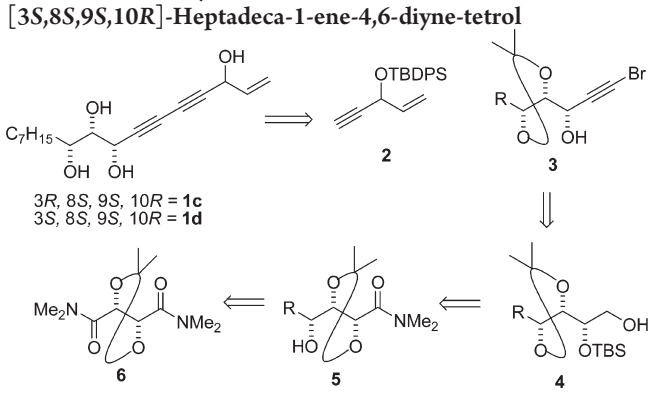
conjugated diyne unit is envisaged through a Cadiot−Chodkiewicz coupling of appropriately protected alkyne triol **3** with either enantiomer of 3-silyloxy-pent-1-en-4-yne **2**. Formation of the alkyne **3** is anticipated from oxidation of alcohol **4** to the aldehyde and subsequent alkynylation. Elaboration of the γ-hydroxy amide **5** derived from the bis-dimethylamide **6** of tartaric acid is planned for the synthesis of **4**.

The synthetic sequence commenced with the addition of 1.5 equiv of *n*-heptylmagnesium bromide to diamide **6**[5] and afforded the γ-oxo-amide **7** in 73% yield (Scheme 2).[6] Reduction of the keto group in **7** with $NaBH_4/CeCl_3$ gave a nonseparable diastereomeric mixture of alcohols in a 95:5 ratio, **5** being the major diastereomer in 90% yield. Conversion of the amide **5** to the methyl ester with *trans* disposition of the acetonide is accomplished in a two-step process. Thus, treatment of **5** with *p*-TSA in benzene at 50 °C resulted the lactone **8** in 80% yield after chromatography. Reaction of the lactone with excess 2,2-dimethoxypropane in the presence of *p*-TSA in dichloromethane afforded **9** in 87% yield.[7] Protection of the hydroxy group in **9** as the silyl ether followed by reduction of the ester with $LiBH_4$ furnished the primary alcohol **4** in 88% yield. Oxidation of **4** with IBX resulted in the aldehyde, which was transformed into the alkynol **11** using Corey−Fuchs[8] protocol and silyl ether deprotection using TBAF. Bromination of **11** with NBS in the presence of catalytic $AgNO_3$ produced the bromoalkyne **3** in 90% yield.

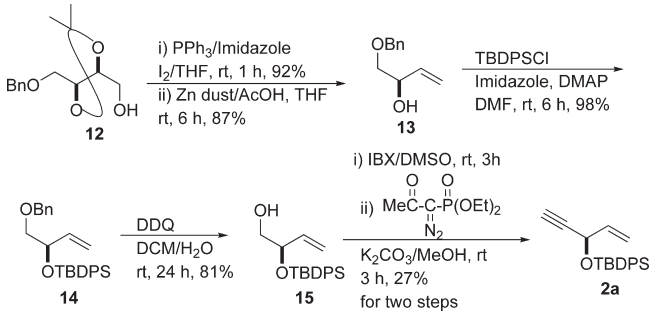
Synthesis of (*R*)-3-silyloxypent-1-en-4-yne is accomplished from the known alcohol **12**[9] as depicted in Scheme 3. Alcohol **12** was converted to the corresponding iodide, which on reaction with zinc dust afforded the allylic alcohol **13** in 87% yield. The free secondary hydroxy group in **13** was protected as the *tert*-butyldiphenylsilyl ether **14**, which on DDQ-mediated debenzylation afforded the primary alcohol **15** in 80% yield. Oxidation of **15** furnished the aldehyde, which on treatment with Ohira−Bestmann reagent[10] yielded (*R*)-3-silyloxypent-1-en-4-yne **2a** (27% for two steps). Similarly, employing the alcohol derived from D-tartaric acid afforded (*S*)-3-silyloxypent-1-en-4-yne **2b**.

Cadiot−Chodkiewicz coupling[11] of the alkynes **3** and **2a** produced the conjugated diyne **16** in 45% yield (Scheme 4).[12] Deprotection of the acetonide and the silyl group in **16** was accomplished by treating the diyne with 4 N HCl in MeOH to afford [3*R*,8*S*,9*S*,10*R*]-heptadeca-1-ene-4,6-diyne-tetrol **1c** in 69% yield. In a similar way the [3*S*,8*R*,9*R*,10*S*]-heptadeca-1-ene-4,6-diyne-tetrol **1d** was prepared by employing **2b** in the

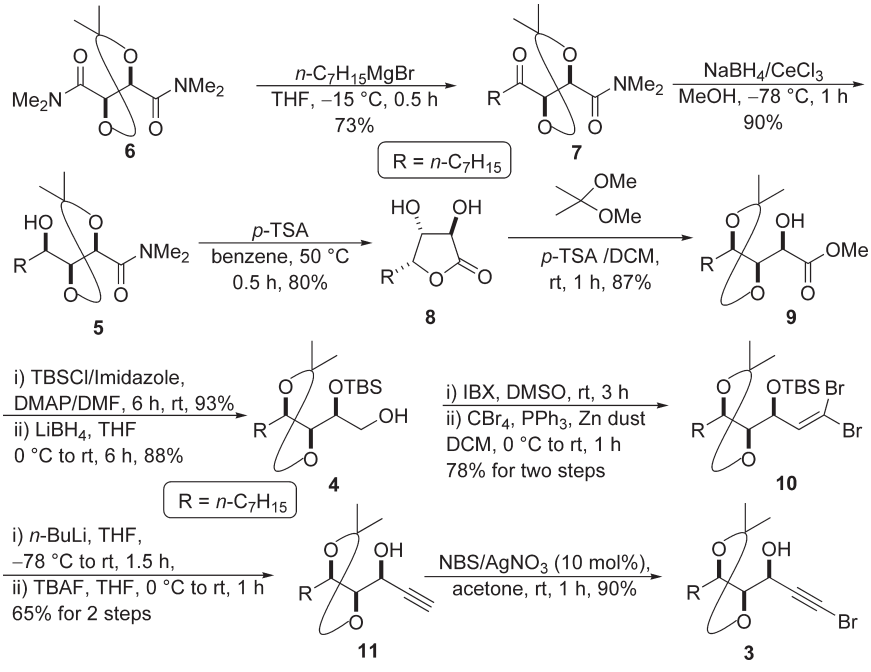
Scheme 1. Retrosynthesis for [3*R*,8*S*,9*S*,10*R*]- and [3*S*,8*S*,9*S*,10*R*]-Heptadeca-1-ene-4,6-diyne-tetrol



Scheme 3. Synthesis of (*R*)-3-Silyloxypent-1-en-4-yne 2a



Scheme 2. Synthesis of Alkyne Triol 3 from Tartaric Acid Diamide



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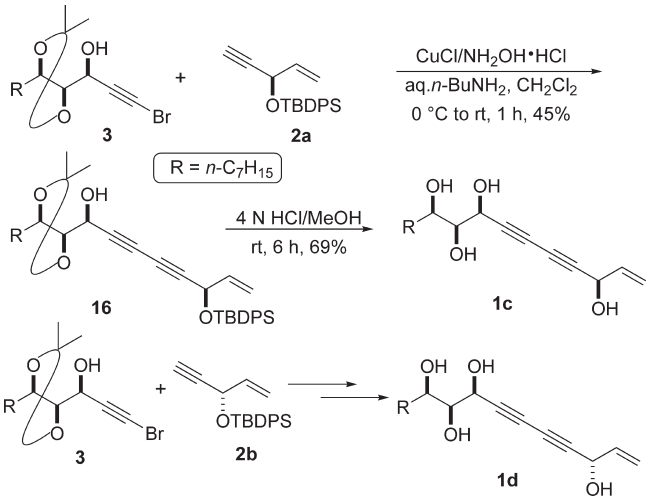
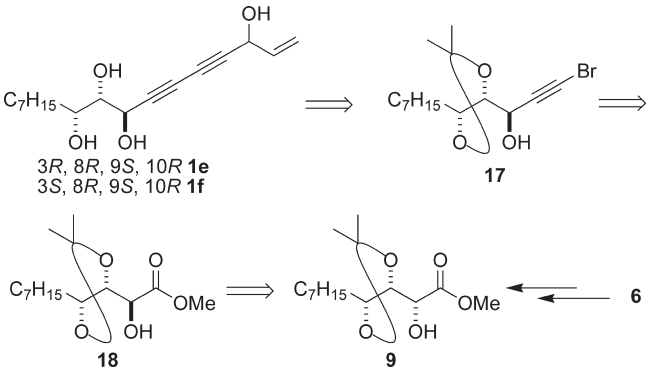
Scheme 4. Synthesis of 3*R*- and 3*S*-[8*S*,9*S*,10*R*]-Heptadeca-1-ene-4,6-diyne-tetrols 1c and 1d



Scheme 5. Retrosynthesis for [3*R*,8*R*,9*S*,10*R*]- and [3*S*,8*R*,9*S*,10*R*]-Heptadeca-1-ene-4,6-diyne-tetrol

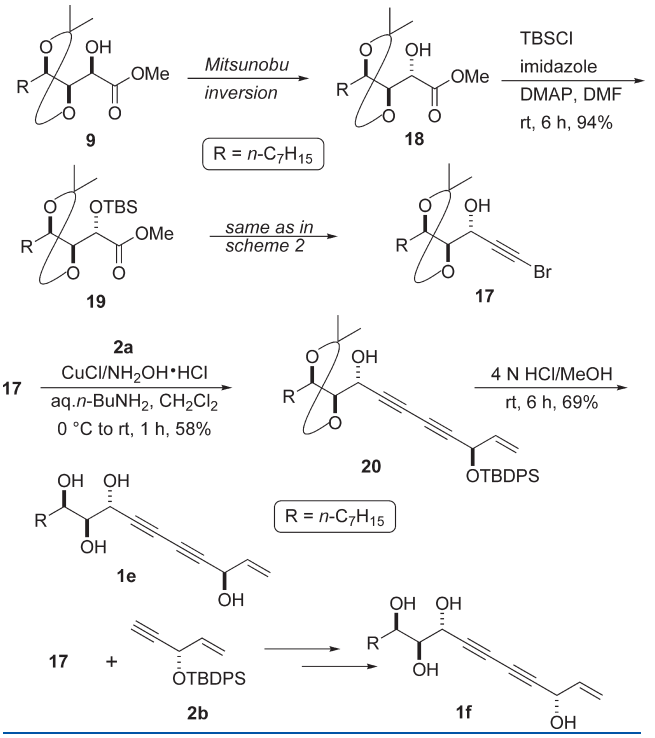


reaction sequence. Unlike the natural product, compound **1d** was not soluble in $CDCl_3$, and neither the spectral data of isomers **1c** and **1d** nor the optical rotations were in agreement with those reported for the natural product.

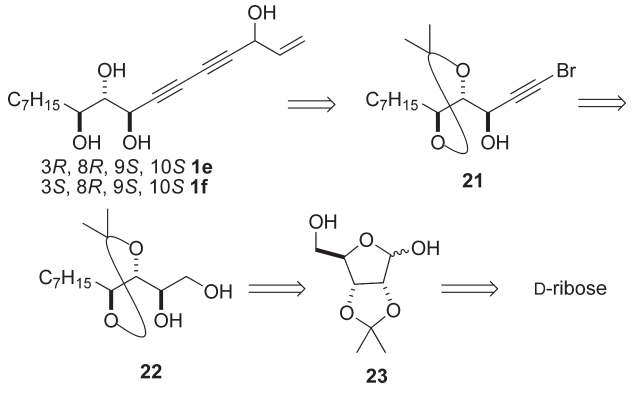
We then turned our attention to the synthesis of [3*R*,8*R*,9*S*,10*R*]-heptadeca-1-ene-4,6-diyne-3,8,9,10-tetrol **1e** and [3*S*,8*R*,9*S*,10*R*]-heptadeca-1-ene-4,6-diyne-3,8,9,10-tetrol **1f**. As depicted in Scheme 5, synthesis of the required alkyne triol unit **17** can be envisaged by the elaboration of the α-hydroxy ester **18**, which in turn can be obtained by Mitsunobu inversion of **9**, the synthesis of which is described in Scheme 2 (*vide supra*).

Accordingly, Mitsunobu inversion[13] of the hydroxy group in **9** afforded the epimeric ester **18** in good yield (Scheme 6). Employing a synthetic sequence similar to that described for the synthesis of **1c** and **1d** (*vide supra*), ester **18** was elaborated to the alkyne triol **17** (see Supporting Information for experimental procedures). Coupling of **17** with **2a** afforded the conjugated diyne **20**, which on deprotection of the protecting groups afforded the diyne tetrol **1e** in 69% yield. Similarly, employing **2b** in the synthetic sequence afforded the other diastereomer **1f**. Contrary to the natural product, **1e** and **1f** are not soluble in $CDCl_3$, and it turned out that the spectral and physical data of the

Scheme 6. Synthesis of 3*R*- and 3*S*-[8*R*,9*S*,10*R*]-Heptadeca-1-ene-4,6-diyne-tetrol 1e and 1f



Scheme 7. Retrosynthesis for [3*R*,8*R*,9*S*,10*S*]- and [3*S*,8*R*,9*S*,10*S*]-Heptadeca-1-ene-4,6-diyne-tetrol



diastereomers **1e** and **1f** are also not in agreement with that reported for the isolated compound.

Realizing the fact that the data of none of the six diastereomers **1a**−**1f** match with that reported, synthesis of the remaining two possible diastereomers 3*R*,8*R*,9*S*,10*S* (**1g**) and 3*S*,8*R*,9*S*,10*S* (**1h**) was planned. For this purpose D-ribose was chosen as the appropriate starting compound possessing the right stereochemistry required for the 8*R*,9*S*,10*S* alkyne triol unit (Scheme 7). Wittig olefination of the lactol **23** with n-$C_6H_{13}PPh_3Br$ was identified as the key reaction for the assembly of the vital triol unit.

Thus, D-ribose was converted to the known lactol **23** employing literature procedure (Scheme 8).[14] Wittig olefination of **23** produced the olefin **24**[15] in 60% yield, which was hydrogenated over Pd/C to yield the diol **22** in 96% yield. Reaction of **22** with Bu_2SnO followed by benzyl bromide resulted in regioselective

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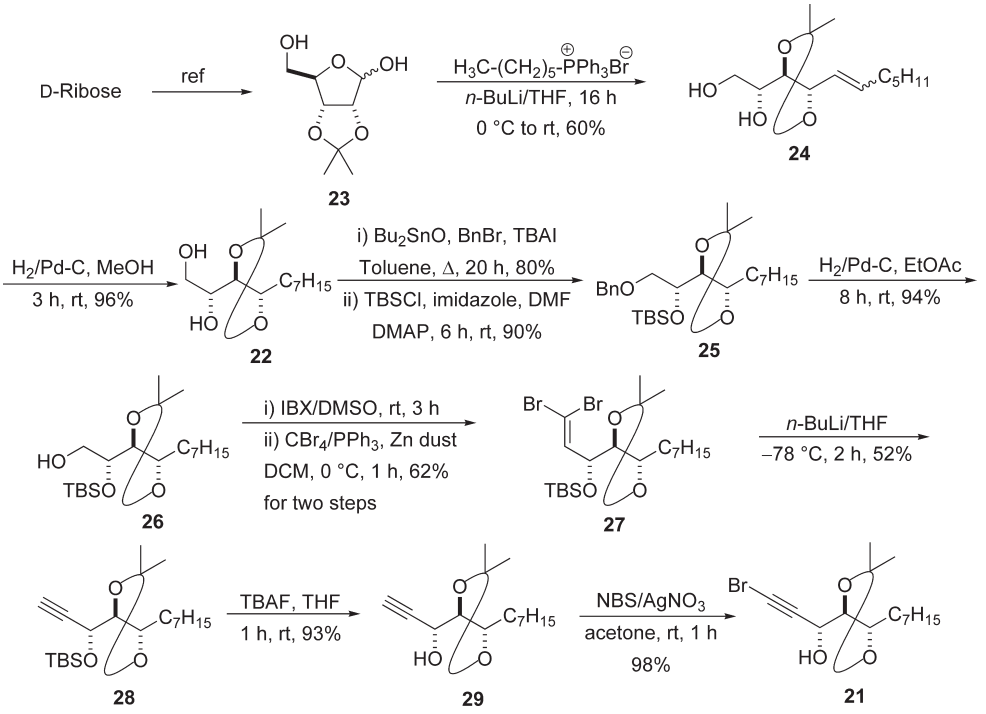
Scheme 8. Synthesis of the Alkynetriol 21 from D-Ribose



benzylation of the primary alcohol, which on treatment with TBDMSCl/imidazole furnished the silyl ether **25** in good yield. Hydrogentaion of **25** over Pd/C afforded the primary alcohol **26** in almost quantitative yield. Oxidation of alcohol **26** furnished the corresponding aldehyde, which was transformed into the alkyne **28** employing Corey−Fuchs protocol. TBAF-mediated deprotection of the silyl ether yielded the alcohol **29**, which on bromination with NBS in the presence of catalytic amount of silver nitrate produced the bromo alkyne **21** in 98% yield.

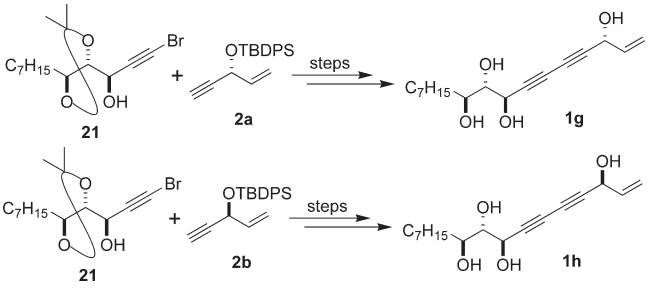
Following a sequence that is described for the synthesis of conjugated diyne tetrols (*vide supra*) alkyne **21** was elaborated to [3*R*,8*R*,9*S*,10*S*]-heptadeca-1-ene-4,6-diyne-tetrol (**1g**) and [3*S*, 8*R*,9*S*,10*S*]-heptadeca-1-ene-4,6-diyne-tetrol (**1h**) (Scheme 9) (see Supporting Information for experimental details).

Neither the spectral data nor the physical data of the diastereomers **1g**−**1h** match with that reported for the natural product. Spectral data and specific rotation of all eight possible diastereomers of heptadec-1-ene-4,6-diyne-3,8,9,10-tetrol are summarized in Table 1 along with those reported for the natural product.

A perusal of the data clearly reveals that the spectral data of the natural product did not match with any of the eight diastereomers [for example, none of the diastereomers exhibited a dt resonance at δ 4.27 in the ^{1}H NMR as reported for the natural product]. Hence it is obvious that the structure assigned for the natural product is not correct and requires revision.

In conclusion, enantioselective synthesis of possible diastereomers of heptadeca-1-ene-4,6-diyne-3,8,9,10-tetrol, a structure proposed for the natural product isolated from *Hydrocotyle leucocephala*, is accomplished. The two alkyne precursors required for the construction of the diyne moiety are synthesized from tartaric acid and D-ribose. The key diyne moiety is assembled *via* copper-catalyzed Cadiot−Chodkiewicz coupling. It was found that the NMR spectral data of the putative structure assigned for the natural product did not match with any of the

Scheme 9. Synthesis of 3*R*- and 3*S*-[8*R*,9*S*,10*S*]-Heptadeca-1-ene-4,6-diyne-tetrol 1g and 1h



diastereomers that were synthesized. This establishes that the structure proposed for the natural product is wrong and requires revision. Perhaps location of the triple bond and/or the four hydroxy groups is in a different position on the heptadecene in the natural product.

EXPERIMENTAL SECTION

Preparation of 7. In an oven-dried two-neck 100 mL, round-bottom flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed **6** (2 g, 8.2 mmol) dissolved in THF (20 mL). The solution was cooled to −15 °C, and *n*-C_7H_{15}MgBr (12.3 mmol, 24.6 mL of 0.5 M solution in THF) was added slowly and stirred for 0.5 h at the same temperature. After the reaction was complete (indicated by TLC), it was cautiously quenched by addition of an ice-cold solution of saturated NH_4Cl (20 mL). The reaction mixture was poured into water (25 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). The residue obtained after removal of the solvent was purified by silica gel column chromatography with EtOAc/petroleum ether (1:4) to yield 7

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Table 1. NMR Spectral Data for Diastereomers (1a−1h) of Heptadec-1-ene-4,6-diyne-3,8,9,10-tetrol

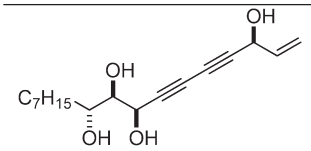
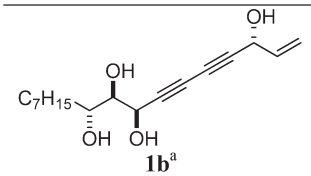
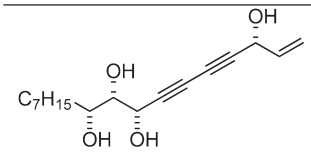
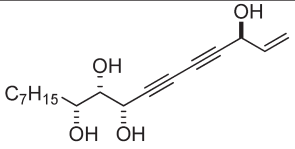
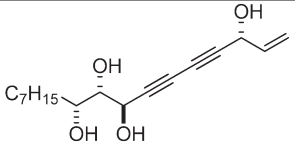
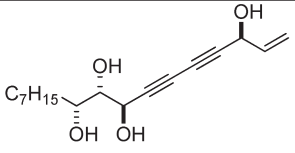
Structure	^{1}H NMR	^{13}C NMR	$[\alpha]_D$
Reported data for the natural product	400 MHz / $CDCl_3$) 5.94 (ddd, 1H, *J* = 17.0, 10.2, 5.2 Hz), 5.48 (d, 1H, *J* = 17 Hz), 5.27 (d, 1H, *J* = 10.2 Hz), 4.94 (d, 1H, *J* = 5.2 Hz), 4.55 (d, 1H, *J* = 6.5 Hz), 4.27 (dt, 1H, *J* = 8.7, 4.0 Hz), 3.74 (dd, 1H, *J* = 6.5, 4.0 Hz), 1.79 (m, 2H), 1.45 (brm, 1H), 1.39 (brm, 1H), 1.29 (m, 8H), 0.88 (brt, 3H, *J* = 7 Hz)	(100 MHz / $CDCl_3$) 135.9, 117.8, 78.7, 78.2, 75.9, 70.9, 70.3, 64.6, 64.6, 63.7, 34.8, 32.0, 29.4, 29.3, 26.7, 22.9, 14.4	+ 5.5 (*c* 1.08, MeOH)
 **1a**[a]	(300 MHz / $CDCl_3$) 5.94 (ddd, 1H, *J* = 16.6, 10.2, 5.2 Hz), 5.47 (d, 1H, *J* = 16.6 Hz), 5.27 (d, 1H, *J* = 10.2 Hz), 4.94 (d, 1H, *J* = 5.2 Hz), 4.68 (d, 1H, *J* = 3.7 Hz), 3.81 (ddd, 1H, *J* = 8.3, 4.5, 4.0 Hz), 3.60 (dd, 1H, *J* = 3.7, 4.5 Hz), 1.65–1.43 (m, 2H), 1.32–1.06 (brm, 10H), 0.88 (brt, 3H, *J* = 6.8 Hz)	(150 MHz / $CDCl_3$) 135.6, 117.4, 78.4, 78.3, 75.6, 72.7, 70.1, 70.0, 63.8, 63.4, 33.1, 31.7, 29.5, 29.2, 25.5, 22.6, 14.0	+ 6.0 (*c* 0.2, MeOH)
 **1b**[a]	(300 MHz / $CDCl_3$) 5.93 (ddd, 1H, *J* = 17.0, 10.2, 5.3 Hz), 5.47 (d, 1H, *J* = 17.0 Hz), 5.25 (d, 1H, *J* = 10.2 Hz), 4.93 (d, 1H, *J* = 5.3 Hz), 4.66 (d, 1H, *J* = 3.5 Hz), 3.80 (ddd, 1H, *J* = 8.1, 4.5, 3.5 Hz), 3.63 (dd, 1H, *J* = 4.5, 3.5 Hz), 1.63–1.44 (m, 2H), 1.36–1.20 (brm, 10H), 0.88 (brt, 3H, *J* = 6.9 Hz)	(75 MHz / $CDCl_3$) 135.7, 117.2, 78.4, 77.1, 75.9, 72.5, 70.1, 70.0, 63.6, 63.1, 32.7, 31.8, 29.5, 29.2, 25.6, 22.6, 14.0	− 20.9 (*c* 0.65, MeOH)
 **1c**	(400 MHz / $CDCl_3$) 5.92 (ddd, 1H, *J* = 16.9, 10.1, 5.3 Hz), 5.46 (d, 1H, *J* = 17.0 Hz), 5.25 (d, 1H, *J* = 10.1 Hz), 4.93 (d, 1H, *J* = 5.2 Hz), 4.56 (d, 1H, *J* = 6.0 Hz), 3.86–3.79 (m, 1H), 3.53 (d, 1H, *J* = 4.8 Hz), 1.60–1.27 (m, 16H), 0.88 (t, 3H, *J* = 7.0 Hz)	(100 MHz /$CDCl_3$) 135.5, 117.2, 78.5, 78.0, 75.6, 71.2, 70.1, 69.8, 64.4, 62.9, 33.8, 31.7, 29.4, 29.1, 25.5, 22.5, 13.9	− 27.6 (*c* 0.6, MeOH)
 **1d**[b]	(400 MHz / CD_3OD) 5.91 (ddd, 1H, *J* = 16.7, 10.1, 5.4 Hz), 5.40 (dd, 1H, *J* = 17.0, 1.1 Hz), 5.19 (dd, 1H, *J* = 10.1, 1.1 Hz), 4.44 (d, 1H, *J* = 7.5 Hz), 3.76 (t, 1H, *J* = 5.8 Hz), 3.38 (d, 1H, *J* = 7.5 Hz), 3.30 (s, 1H), 1.57–1.33 (m, 12H), 0.90 (t, 3H, *J* = 6.5 Hz)	(100 MHz / CD_3OD) 138.0, 116.6, 79.9, 79.6, 77.6, 72.0, 70.4, 70.0, 65.4, 63.8, 34.9, 33.0, 30.7, 30.4, 26.9, 23.7, 14.4	+ 34.4 (*c* 1.4, MeOH)
 **1e**[b]	(400 MHz / CD_3OD) 5.92 (ddd, 1H, *J* = 16.7, 10.1, 5.5 Hz), 5.40 (d, 1H, *J* = 17.0 Hz), 5.19 (d, 1H, *J* = 10.0 Hz), 4.43 (d, 1H, *J* = 7.3 Hz), 3.82–3.70 (m, 1H), 3.38 (brd, 1H, *J* = 7.5 Hz), 3.32 (brs, 1H), 1.53–1.32 (m, 12H), 0.90 (t, 3H, *J* = 7.0 Hz)	(100 MHz / CD_3OD) 138.1, 116.6, 81.4, 78.9, 76.6, 71.0, 70.4, 69.5, 64.6, 63.8, 34.5, 33.0, 30.7, 30.4, 26.9, 23.7, 14.4	− 31.7 (*c* 1.5, MeOH)
 **1f**[b]	(400 MHz / CD_3OD) 5.90 (ddd, 1H, *J* = 16.9, 10.1, 5.5 Hz), 5.39 (d, 1H, *J* = 17.0 Hz), 5.18 (d, 1H, *J* = 10.1 Hz), 4.42 (d, 1H, *J* = 7.3 Hz), 3.84–3.75 (m, 1H), 3.37 (dd, 1H, *J* = 7.3, 2.4 Hz), 3.30 (s, 1H), 1.57–1.30 (m, 12H), 0.90 (t, 3H, *J* = 6.9 Hz)	(100 MHz / CD_3OD) 136.6, 115.1, 80.0, 77.5, 75.2, 69.6, 68.9, 68.1, 63.2, 62.4, 33.1, 31.6, 29.3, 29.0, 25.5, 22.3, 13.0	+ 28.2 (*c* 1.1, MeOH)

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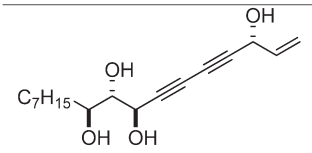
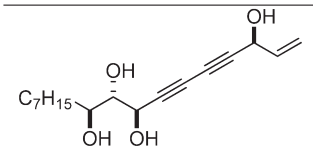
Table 1. Continued

Structure	^{1}H NMR	^{13}C NMR	$[\alpha]_D$
 **1g**	(400 MHz / $CDCl_3$) 5.91 (ddd, 1H, *J* = 16.6, 10.1, 5.3 Hz), 5.46 (d, 1H, *J* = 16.9 Hz), 5.24 (d, 1H, *J* = 10.1 Hz), 4.93 (d, 1H, *J* = 4.4 Hz), 4.75 (brs, 1H), 4.52 (brs, 1H), 3.98 (brs, 1H), 3.68–3.65 (brm, 2H), 3.42 (brs, 1H), 1.76–1.27 (m, 12H), 0.88 (t, 3H, *J* = 6.9 Hz)	(100 MHz / $CDCl_3$) 135.6, 117.4, 78.4, 78.1, 76.4, 72.9, 70.5, 70.2, 64.7, 63.1, 33.3, 31.9, 29.7, 29.4, 25.6, 22.6, 14.1	– 41.7 (*c* 2.3, MeOH)
 **1h**[b]	(400 MHz / CD_3OD) 5.91 (ddd, 1H, *J* = 16.9, 10.1, 5.5 Hz), 5.40 (d, 1H, *J* = 17.0 Hz), 5.19 (d, 1H, *J* = 10.1 Hz), 4.64 (d, 1H, *J* = 3.9 Hz), 3.56–3.52 (m, 1H), 3.44 (dd, 1H, *J* = 8.1, 4.0 Hz), 3.31 (brs, 1H), 1.78–1.32 (m, 12H), 0.91 (t, 3H, *J* = 6.9 Hz)	(100 MHz / CD_3OD) 138.1, 116.6, 79.9, 78.8, 78.4, 73.1, 70.5, 70.2, 65.6, 63.8, 34.2, 33.0, 30.8, 30.5, 26.4, 23.7, 14.4	+ 11.9 (*c* 1.4, MeOH)

[a] From ref 4. [b] In contrast to the reported data, these isomers are not soluble in $CDCl_3$ and the spectra is recorded in CD_3OD.

(1.79 g, 73%) as a colorless oil. R_f 0.5 (2:3 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +14.6 (*c* 3.50, $CHCl_3$); IR (neat) 2930, 1716, 1653, 1374, 1058 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.12 (d, 1H, *J* = 5.6 Hz), 4.79 (d, 1H, *J* = 5.6 Hz). 3.13 (s, 3H), 2.97 (s, 3H), 2.71−2.55 (m, 2H), 1.62−1.53 (m, 2H), 1.41 (s, 6H), 1.27 (brm, 8H), 0.85 (t, 3H, *J* = 6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.4, 168.1, 112.0, 82.0, 74.8, 39.4, 36.9, 35.9, 31.5, 29.0, 28.9, 26.3, 26.0, 23.0, 22.5, 14.0; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{16}H_{29}NO_4$, 322.1994; found, 322.1990.

Preparation of 5. To a solution of **7** (1.6 g, 5.4 mmol) in MeOH (25 mL) was added $CeCl_3 \cdot 7H_2O$ (4.02 g, 10.8 mmol), and the mixture was stirred for 1 h. $NaBH_4$ (0.41 g, 10.8 mmol) was then added portionwise at −78 °C and stirred at the same temperature for 1 h. After the reaction was complete (TLC), it was quenched by the addition of water (1 mL). Most of the volatiles were removed under reduced pressure, and the solid residue thus obtained was dissolved in 1 N HCl (8 mL) and extracted with diethyl ether (3 × 10 mL). The combined ethereal layers were washed with brine (10 mL), dried over Na_2SO_4, and concentrated. The crude residue obtained was purified by silica gel column chromatography with EtOAc/petroleum ether (3:7) to give the alcohol **5** in 90% (1.45 g) yield as a colorless oil. R_f 0.5 (1:1 EtOAc/petroleum ether); $[\alpha]^{26}_D$ −10.8 (*c* 2.30, $CHCl_3$); IR (neat) 3447, 2986, 2930, 2857, 1651, 1380 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.49−4.48 (m, 2H), 3.53−3.50 (m, 1H), 3.07 (s, 3H), 2.89 (s, 3H), 1.99 (d, 1H, *J* = 9.3 Hz), 1.47−1.20 (m, 18H), 0.80 (t, 3H, *J* = 7.5 Hz) ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 110.1, 80.1, 74.1, 69.9, 37.0, 35.9, 35.6, 34.7, 31.7, 29.4, 29.1, 26.7, 25.8, 22.6, 14.0; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{16}H_{31}NO_4$, 324.2151; found, 324.2161.

Preparation of 8. To a solution of **5** (1.09 g, 3.65 mmol) in benzene (15 mL) was added *p*-toluenesulphonic acid (0.69 g, 3.65 mmol), and the mixture was heated to 50 °C. After 0.5 h the reaction mixture was cooled to room temperature, and K_2CO_3 (0.5 g) was added. After stirring for 15 min, the mixture was filtered through a short pad of Celite, and the Celite pad was washed with diethyl ether (20 mL). Evaporation of solvent followed by silica gel column chromatography of the resultant residue with EtOAc/petroleum ether (2:3) gave **8** (0.63 g, 80%) as a white solid. R_f 0.4 (3:2 EtOAc/petroleum ether); mp 75−77 °C; $[\alpha]^{26}_D$ +128.9 (*c* 1.20, $CHCl_3$); IR (KBr) 3403, 2955, 2925, 2856, 1773, 1465 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.96 (brs, 1H), 4.51−3.97 (m, 2H), 2.68 (brs, 1H), 1.77−1.74 (m, 1H), 1.49−1.20 (m, 12H), 0.81 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 81.4, 73.6, 72.9, 31.7, 29.3, 29.1, 28.9, 25.6, 22.6, 14.0; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{11}H_{20}O_4$, 239.1259; found, 239.1257.

Preparation of 9. To a stirred solution of the lactone **8** (0.7 g, 3.25 mmol) in CH_2Cl_2 (10 mL) were added *p*-toluenesulphonic acid (62 mg, 0.32 mmol) and 2,2-dimethoxy propane (0.8 mL, 6.5 mmol). The reaction mixture was stirred at room temperature for 1 h and after completion of the reaction (TLC), K_2CO_3 (45 mg) was added and stirred for 15 min. The reaction mixture was then passed through a pad of Celite, and the Celite pad was washed with diethyl ether (20 mL). Evaporation of solvent followed by silica gel column chromatography of the resultant residue with petroleum ether/EtOAc (9:1) as eluent afforded α-hydroxy ester **9** in 87% (0.81 g) yield. R_f 0.6 (1:4 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +18.4 (*c* 3.00, $CHCl_3$); IR (neat) 3491, 2987, 2930, 2857, 1749, 1253 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10−4.08 (m, 2H), 3.87 (dd, 1H, *J* = 8.3, 1.2 Hz), 3.83 (s, 3H), 3.02 (d, 1H, *J* = 9.1 Hz), 1.65−1.45 (m, 3H), 1.42−1.23 (m, 15 H), 0.88 (t, 3H, *J* = 7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 109.0, 81.3, 76.3, 68.7, 52.6, 32.4, 31.6, 29.5, 29.0, 27.3, 26.4, 25.8, 22.5, 13.9; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{15}H_{28}O_5$, 311.1834; found, 311.1839.

Preparation of 4. To a stirred solution of **9** (1.16 g, 4.02 mmol) in dry DMF (4 mL) were added imidazole (0.82 g, 12 mmol) and DMAP (99 mg, 0.8 mmol). After 15 min of stirring at room temperature, TBDMSCl (1.2 g, 8.04 mmol) was introduced into the reaction mixture, which was stirred at room temperature for 6 h. The reaction mixture was then poured into water (10 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried (Na_2SO_4). Evaporation of solvent followed by silica gel column chromatography of the crude residue with petroleum ether/EtOAc (95:5) as eluent afforded the silyl ether as a colorless oil in 93% (1.51 g) yield. R_f 0.6 (1:9 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +38.1 (*c* 1.10, $CHCl_3$); IR (neat) 2953, 2930, 2858, 1761, 1749, 1253 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.25 (d, 1H, *J* = 3.2 Hz), 4.07 (dt, 1H, *J* = 7.7, 5.8 Hz), 3.89 (dd, 1H, *J* = 7.9, 3.3 Hz), 3.75 (s, 3H), 1.67−1.22 (m, 18H), 0.92 (s, 9H), 0.88 (t, 3H, *J* = 7.0 Hz), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 109.0, 82.0, 76.5, 71.7, 52.0, 33.2, 31.8, 29.7, 29.2, 27.5, 26.6, 26.1, 25.7, 22.7, 18.4, 14.1, −4.9, −5.3; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{21}H_{42}O_5Si$, 425.2699; found, 425.2696.

In an oven-dried 100 mL two-neck round-bottom flask equipped with magnetic stir bar, rubber septum, and argon balloon was placed the silyloxyester (0.95 g, 2.36 mmol) (prepared above) dissolved in 10 mL of THF and cooled to 0 °C. $LiBH_4$ (1.1 mL, 2 M solution in THF, 2.36 mmol) was added slowly to the reaction mixture. After the addition was over the mixture was warmed to room temperature and stirred for

another 6 h at room temperature. It was then cautiously quenched by addition of saturated NH_4Cl solution (5 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Evaporation of the solvent and silica gel column chromatography of the resultant residue with petroleum ether/EtOAc (17:3) yielded **4** (0.77 g, 88%) as a colorless oil. R_f 0.5 (3:7 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +15.4 (*c* 3.80, $CHCl_3$); IR (neat) 3490, 2953, 2930, 2858, 1376, 1253, 1062 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.98 (dt, 1H, *J* = 11.3, 3.1 Hz), 3.82−3.79 (m, 1H), 3.73−3.59 (m, 3H), 2.25 (t, 1H, *J* = 6 Hz), 1.64−1.47 (m, 4H), 1.37 (m, 6H), 1.27−1.25 (m, 8H), 0.89 (s, 9H), 0.86 (t, 3H, *J* = 7.0 Hz), 0.11−0.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.3, 82.2, 76.9, 71.5, 64.1, 33.4, 31.8, 29.6, 29.1, 27.3, 26.8, 26.2, 25.8, 22.6, 18.1, 14.0, −4.60, −4.67; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{20}H_{42}O_4Si$, 397.2750; found, 397.2746.

Preparation of 10. A solution of the alcohol **4** (0.82 g, 2.21 mmol) dissolved in DMSO (10 mL) was cooled to 0 °C, and IBX (0.92 g, 3.3 mmol) was introduced. The reaction mixture was then warmed to room temperature and stirred for 3 h. After the reaction was over (indicated by TLC), it was cooled to 0 °C and quenched with the addition of ice-cold water (5 mL). The solids were removed by filtering through a short pad of Celite, and the Celite pad was washed with diethyl ether (20 mL). The filtrate was extracted with ether (20 mL). Combined ethereal extracts were washed with brine (30 mL) and dried (Na_2SO_4). Evaporation of the solvent gave the crude aldehyde which was subjected to the next reaction without further purification.

To a solution of the crude aldehyde obtained above in dry CH_2Cl_2 (10 mL) were added CBr_4 (2.93 g, 2.6 mmol) and zinc dust (0.57 g, 2.6 mmol). The reaction mixture was cooled to 0 °C, and PPh_3 (2.32 g, 2.6 mmol) was added portionwise. After the addition was over, the mixture was was stirred at 0 °C for 1 h. After completion of the reaction (TLC) the mixture was diluted with hexane and filtered through a short pad of Celite, and the Celite pad was washed with diethyl ether (20 mL). Evaporation of the solvent and purification of the crude residue thus obtained by silica gel column chromatography with petroleum ether/EtOAc (98:2) gave **10** (0.91 g, 78% yield over two steps) as an oil. R_f 0.6 (5:95 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +24.4 (*c* 1.90, $CHCl_3$); IR (neat) 2986, 2955, 2930, 2858, 1253 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.58 (d, 1H, *J* = 10.5 Hz), 4.45 (dd, 1H, *J* = 8.5, 3.7 Hz), 4.04 (dt, 1H, *J* = 13.5, 6.1 Hz), 3.70 (dd, 1H, *J* = 7.8, 3.7 Hz), 1.66−1.38 (m, 18H), 0.98−0.92 (m, 12H), 0.16−0.15 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 109.0, 90.3, 83.3, 76.5, 73.2, 33.6, 31.8, 29.6, 29.2, 27.6, 26.7, 26.0, 25.8, 22.7, 18.1, 14.1, −4.4, −4.9; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{21}H_{40}Br_2O_3Si$, 551.1098; found, 551.1058.

Preparation of 11. To a solution of **10** (0.68 g, 1.3 mmol) in dry THF (10 mL) was slowly added *n*-BuLi (1.5 mL, 3.3 mmol, 2.6 M in THF) at −78 °C, and the mixture was stirred at the same temperature for 30 min. The reaction mixture was warmed to 0 °C and stirred for another 0.5 h. It was allowed to come to room temperature and stirred for 0.5 h. Then it was cooled to 0 °C and cautiously quenched with water (5 mL). The reaction mixture was extracted with diethyl ether (3 × 10 mL) and the ethereal extracts were washed with brine (10 mL) and dried over Na_2SO_4. Evaporation of the solvent followed purification of the resulting residue by silica gel column chromatography with petroleum ether/EtOAc (98:2) as eluent afforded the alkyne as a colorless oil.

To a precooled (0 °C) solution of the silyloxy alkyne (obtained above) in THF (5 mL) was added TBAF (2.6 mL of 1 M in THF, 2.6 mmol), and the mixture was stirred at room temperature. After 1 h the reaction mixture was quenched with water (5 mL) and extracted with diethyl ether (3 × 10 mL). Combined organic layers were washed with brine and then dried over Na_2SO_4. Evaporation of the solvent and purification with silica gel column chromatography with petroleum ether/EtOAc (9:1) gave the alcohol **11** (0.21 g, 65% yield) as a colorless oil. R_f 0.6 (1:4 EtOAc/petroleum ether); $[\alpha]^{26}_D$ −25.3 (*c* 1.10, $CHCl_3$); IR (neat) 3436, 3311, 2985, 2929, 2859, 1599, 1380 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.32 (m, 1H), 3.96 (dt, 1H, *J* = 7.9, 3.9 Hz), 3.75 (dd, 1H, *J* = 7.5, 4.9 Hz), 2.61−2.45 (m, 2H), 1.77−1.27 (m, 18H), 0.87 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.1, 82.7, 81.2, 77.2, 74.0, 62.3, 33.3, 31.4, 29.2, 28.8, 27.2, 26.7, 25.6, 22.3, 13.7; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{15}H_{26}O_3$, 277.1780; found, 277.1775.

Preparation of 3. To a stirred solution of the alkyne **11** (0.2 g, 0.8 mmol) in dry acetone (5 mL) were added NBS (0.28 g, 1.6 mmol) and $AgNO_3$ (14 mg, 0.08 mmol), and the mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with hexane and filtered through a pad of Celite, and the Celite pad was washed with diethyl ether (10 mL). Residue obtained after evaporation of the solvent was purified by silica gel column chromatography with petroleum ether/ethyl acetate (9:1) as eluent to afford **3** as a colorless oil (0.24 g) in 90% yield. R_f 0.6 (1:4 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +10.1 (*c* 1.00, $CHCl_3$); IR (neat) 3423, 2986, 2929, 2858, 1375, 1249 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.36 (t, 1H, *J* = 5.8 Hz), 3.94 (dt, 1H, *J* = 7.7, 4.0 Hz), 3.74 (dd, 1H, *J* = 7.4, 5.2 Hz), 2.53 (d, 1H, *J* = 6.5 Hz), 1.71−1.54 (m, 3H), 1.43 (s, 3H), 1.40 (s, 3H), 1.36−1.24 (m, 9H), 0.88 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.5, 83.2, 77.7, 76.6, 63.8, 46.9, 33.6, 31.7, 29.5, 29.1, 27.5, 27.0, 25.9, 22.6, 14.0; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{15}H_{25}BrO_3$, 355.0885; found, 355.0876.

Preparation of 13. To a solution of the monobenzyl alcohol **12** (1.11 g, 4.4 mmol) in THF (12 mL) were added imidazole (0.46 g, 6.6 mmol), triphenylphosphine (1.8 g, 6.6 mmol), and iodine (1.73 g, 6.6 mmol) sequentially, and the mixture was stirred at room temperature for 1 h. After the reaction was complete (indicated by TLC), it was quenched with water (5 mL) and extracted with diethyl ether (20 × 3 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). The residue thus obtained after removal of the solvent was purified by silica gel column chromatography to yield the iodide (1.46 g, 92%) as a colorless oil. R_f 0.5 (5:95 EtOAc/petroleum ether); $[\alpha]^{26}_D$ −8.6 (*c* 2.50, $CHCl_3$); IR (neat) 3087, 3063, 3029, 2986, 2865, 1453, 1371, 1215, 1094 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.25 (m, 5H), 4.58 (s, 2H), 3.96 (dt, 1H, *J* = 7.2, 4.8 Hz), 3.86 (dt, 1H, *J* = 7.5, 5.4 Hz), 3.65 (d, 1H, *J* = 1.8 Hz), 3.64 (d, 1H, *J* = 1.5 Hz), 3.34 (dd, 1H, *J* = 10.8, 5.1 Hz), 3.24 (dd, 1H, *J* = 10.8, 5.1 Hz), 1.46 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 137.7, 128.3, 127.7, 127.6, 109.7, 80.0, 76.5, 73.5, 70.4, 27.3, 27.2, 6.3; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{14}H_{19}IO_3$, 385.0277; found, 385.0261.

To a solution of the iodide (prepared above) in THF were added zinc dust (2.16 g, 33.2 mmol) and AcOH (2.4 mL, 41.5 mmol), and the mixture was stirred at room temperature. Progress of the reaction was monitored by TLC, and after reaction was complete (∼6 h) the solid residue was filtered through a Celite pad, and the Celite pad was washed with ether (40 mL). The filtrate was diluted with water (10 mL) and then extracted with ether (3 × 10 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). The residue obtained after removal of the solvent was purified by silica gel column chromatography to yield **13** (64 g, 87%) as a colorless oil. R_f 0.5 (3:17 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +5.0 (*c* 1.80, $CHCl_3$); IR (neat) 3432, 2860, 1453, 1105 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35−7.29 (m, 5H), 5.80 (ddd, 1H, *J* = 17.4, 10.8, 5.7 Hz), 5.35 (dt, 1H, *J* = 17.4, 1.5 Hz), 5.19 (dt, 1H, *J* = 10.8, 1.5 Hz), 4.56 (s, 2H), 4.37−4.31 (m, 1H), 3.53 (dd, 1H, *J* = 9.6, 3.3 Hz), 3.37 (dd, 1H, *J* = 9.6, 7.8 Hz), 2.62 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.8, 136.5, 128.4, 127.8, 127.7, 116.4, 74.0, 73.3, 71.4; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{11}H_{14}O_2$, 201.0891; found, 201.0899.

Preparation of 14. To a stirred solution of **13** (0.62 g, 2.5 mmol) in dry DMF (2 mL) were added imidazole (0.72 g, 10.5 mmol) and DMAP (86 mg, 0.7 mmol). After 15 min of stirring at room temperature, TBDPSCl (1.8 mL, 7 mmol) was introduced into the reaction mixture, and the mixture was stirred at room temperature for 6 h. The reaction mixture was then poured into water (10 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried (Na_2SO_4). Evaporation of solvent followed by silica

gel column chromatography of the crude residue with petroleum ether/ethyl acetate (98:2) as eluent afforded the silyl ether **14** (1.43 g, 98%) as a colorless oil. R_f 0.6 (5:95 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +27.7 (*c* 2.70, $CHCl_3$); IR (neat) 3070, 2932, 2858, 1111 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74−7.67 (m, 4H), 7.44−7.21 (m, 11H), 5.93 (ddd, 1H, *J* = 17.4, 10.8, 6.0 Hz), 5.24 (dt, 1H, *J* = 17.4, 1.5 Hz), 5.12 (dt, 1H, *J* = 10.2, 1.5 Hz), 4.41−4.35 (m, 3H), 3.47 (dd, 1H, *J* = 9.9, 5.7 Hz), 3.39 (dd, 1H, *J* = 9.9, 5.7 Hz), 1.11 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 136.0, 135.9, 134.2, 133.8, 129.5, 128.2, 127.5, 127.4, 115.5, 74.6, 73.3, 73.1, 27.0, 19.3; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{27}H_{32}O_2Si$, 439.2069; found, 439.2060.

Preparation of 15. To a solution of **14** (1.1 g, 2.65 mmol) in a 10:1 mixture of CH_2Cl_2/H_2O (20 mL) was added DDQ (3 g, 13.3 mmol), and the mixture was stirred at room temperature for 24 h. After the reaction was complete (indicated by TLC), the reaction mixture was passed through a pad of Celite, and the Celite pad was washed with ether (40 mL). The filtrate was washed with a saturated solution of $NaHCO_3$ (2 × 10 mL) and brine (10 mL), dried over Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography using petroleum ether/ethyl acetate (4:1) as eluent to yield the alcohol **15** in 81% (0.7 g) yield as a colorless oil. R_f 0.5 (1:9 EtOAc/petroleum ether); $[\alpha]^{26}_D$ −7.0 (*c* 3.10, $CHCl_3$); IR (neat) 3422, 2932, 2858, 1427, 1110 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71−7.68 (m, 4H), 7.45−7.37 (m, 6H), 5.83 (ddd, 1H, *J* = 16.8, 10.5, 6.2 Hz), 5.17−5.09 (m, 2H), 4.28 (m, 1H), 3.50 (t, 2H, *J* = 5.6 Hz), 1.82 (t, 1H, *J* = 6.3 Hz), 1.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 135.8, 135.6, 133.7, 133.3, 129.8, 129.7, 127.6, 127.5, 116.6, 75.1, 66.5, 26.9, 19.3; HRMS (*m*/*z*) - $[M + Na]^+$ calcd for $C_{20}H_{26}O_2Si$, 349.1600; found, 349.1615.

Preparation of 2a. The alcohol **15** (1.5 g, 4.6 mmol) dissolved in DMSO (8 mL) was cooled to 0 °C, and IBX (2.6 g, 9.2 mmol) was added to it. The reaction mixture was warmed to room temperature and stirred for 3 h. After the reaction was over, the mixture was cooled to 0 °C and was quenched with ice-cold water (8 mL). The solids were filtered through a short pad of Celite, and the Celite pad was washed with diethyl ether (20 mL). The filtrate was extracted with ether (20 mL). Combined ethereal extracts were washed with brine (30 mL) and dried (Na_2SO_4). Evaporation of the solvent gave the crude aldehyde, which was subjected to the next reaction without further purification.

To a solution of the aldehyde in dry methanol (10 mL) was added a dissolved solution of Ohira−Bestmann reagent (2.02 g, 9.2 mmol) in MeOH (5 mL), and the mixture was cooled to 0 °C. Then K_2CO_3 (1.27 g, 9.2 mmol) was introduced into the reaction mixture, which was stirred at room temperature for another 3 h. After reaction was complete (TLC), the reaction mixture was diluted with hexane (5 mL) and filtered through a short pad of Celite, and the Celite pad was washed with diethyl ether (10 mL). Evaporation of the solvent and silica gel column chromatography of the residue with petroleum ether/EtOAc (98:2) as eluent afforded the alkyne **2a** in 27% (0.39 g) yield as a colorless oil. R_f 0.7 (2:98 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +46.8 (*c* 1.10, $CHCl_3$) [lit. $[\alpha]_D$ +45.6 (*c* 2.9, $CHCl_3$)]; IR (neat) 3304, 2959, 2859, 1428, 1111, 1069 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77−7.67 (m, 4H), 7.45−7.34 (m, 6H), 5.89 (ddd, 1H, *J* = 17.1, 10.2, 5.1 Hz), 5.32 (dt, 1H, *J* = 16.8, 1.5 Hz), 5.12 (dd, 1H, *J* = 10.5, 1.5 Hz), 4.82 (m, 1H), 2.44 (d, 1H, *J* = 2.1 Hz), 1.09 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1, 136.0, 135.8, 133.2, 133.1, 129.8, 127.6, 127.5, 115.6, 83.0, 73.8, 64.3, 26.8, 19.3; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{21}H_{24}OSi$, 343.1494; found, 343.1484.

Preparation of 16. To a stirred solution of *n*-$BuNH_2$ (4.7 mL, 48 mmol) and distilled water (11 mL) was added Cu(I) chloride (10 mg, 0.1 mmol) under a flow of N_2 at 0 °C, which resulted in a deep blue solution. A few crystals of $NH_2OH \cdot HCl$ were added to get a colorless solution, which is indicative of the presence of the required Cu(I) salt. A solution of **2a** (0.17 g, 0.53 mmol) in CH_2Cl_2 (5 mL) was added at 0 °C resulting in a yellow suspension. Then **3** (0.19 g, 0.58 mmol) in CH_2Cl_2 was slowly added ($NH_2OH \cdot HCl$ should be added whenever color of the reaction mixture turns blue). The reaction mixture was allowed to warm to room temperature. After stirring for 1 h, the solution was extracted with CH_2Cl_2 (3 × 10 mL), dried over Na_2SO_4, and concentrated in vacuo. The crude product was purified by column chromatography using petroleum ether/EtOAc (95:5) to yield the desired product **16** (0.15 g) in 45% yield. R_f 0.4 (1:9 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +131.3 (*c* 2.70, $CHCl_3$); IR (neat) 3420, 2985, 2954, 2930, 2858, 1372, 1249, 1113, 1059 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69−7.60 (m, 4H), 7.38−7.21 (m, 6H), 5.79 (ddd, 1H, *J* = 16.7, 10.1, 5.4 Hz), 5.23 (d, 1H, *J* = 16.9 Hz), 5.08 (d, 1H, *J* = 10.1 Hz), 4.79 (d, 1H, *J* = 5.3 Hz), 4.35 (brs, 1H), 3.90 (dt, 1H, *J* = 7.7, 4.1 Hz), 3.69 (dd, 1H, *J* = 7.5, 4.7 Hz), 2.47 (brs, 1H), 1.60−1.22 (m, 18 H), 1.04−1.02 (m, 9H), 0.82 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.2, 135.9, 135.7, 133.0, 132.8, 129.9, 127.62, 127.60, 116.1, 109.5, 83.0, 79.1, 77.6, 70.3, 69.4, 64.9, 63.2, 33.5, 31.7, 29.5, 29.1, 27.5, 27.0, 26.8, 26.5, 25.9, 22.6, 19.3, 14.0; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{36}H_{48}O_4Si$, 595.3223; found, 595.3220.

Preparation of 1c. To a solution of **16** (17 mg, 0.03 mmol) in MeOH (1 mL) was added 4 N HCl (1 mL), and the mixture was stirred at room temperature for 6 h. After reaction was over (indicated by TLC), MeOH was removed under reduced pressure, water (5 mL) was added, and the mixture was extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent and purification of the crude residue by silica gel column chromatography using petroleum ether/EtOAc (7:3) gave the diyne tetrol **1c** in 69% (6 mg) yield as yellow oil. R_f 0.5 (3:2 EtOAc/petroleum ether); $[\alpha]^{26}_D$ −27.6 (*c* 0.60, MeOH); IR (neat) 3368, 2927, 2858, 1662, 1457, 1024 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3 + D_2O$) δ 5.92 (ddd, 1H, *J* = 16.9, 10.1, 5.3 Hz), 5.46 (d, 1H, *J* = 17.0 Hz), 5.25 (d, 1H, *J* = 10.1 Hz), 4.93 (d, 1H, *J* = 5.2 Hz), 4.56 (d, 1H, *J* = 6.0 Hz), 3.86−3.79 (m, 1H), 3.53 (d, 1H, *J* = 4.8 Hz), 1.60−1.27 (m, 16H), 0.88 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 117.2, 78.5, 78.0, 75.6, 71.2, 70.1, 69.8, 64.4, 62.9, 33.8, 31.7, 29.4, 29.1, 25.5, 22.5, 13.9; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{17}H_{26}O_4$, 317.1729; found, 317.1714.

Preparation of 18. To a precooled (0 °C) solution of **9** (0.5 g, 1.74 mmol) in dry THF (20 mL) were added triphenylphosphine (1.83 g, 6.96 mmol) and *p*-nitro benzoic acid (1.16 g, 6.96 mmol mmol) under argon atmosphere, and the mixture was stirred for 10 min. DIAD (1.4 mL, 6.96 mmol) was introduced into the reaction mixture over a period of 20 min at the same temperature. The reaction mixture was warmed to room temperature and stirred for 5 h. After the reaction was complete (TLC), the solvent was removed under reduced pressure, and the crude ester thus obtained was purified by column chromatography to yield the corresponding *p*-nitro benzoate ester (0.67 g, 87%) as pale yellow oil. R_f 0.5 (1:9 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +23.5 (*c* 1.60, $CHCl_3$); IR (neat) 2930, 2857, 1736, 1531 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.34−8.27 (m, 4H), 5.46 (d, 1H, *J* = 3.0 Hz), 4.30−4.26 (m, 1H), 4.15 (dd, 1H, *J* = 7.8, 3.1 Hz), 3.82 (s, 3H), 1.61−1.27 (m, 18H), 0.88 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 163.8, 134.2, 130.9, 123.5, 109.6, 79.6, 77.0, 72.9, 52.6, 33.2, 31.7, 29.4, 29.0, 27.4, 26.7, 25.8, 22.5, 13.9; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{22}H_{31}NO_8$, 460.1947; found, 460.1960.

To a solution of the benzoate (obtained above) (0.71 g, 1.63 mmol) in methanol (10 mL) was added K_2CO_3 (0.23 g) at 0 °C, and the mixture was stirred for 15 min. The reaction mixture was then filtered through a short pad of Celite. The Celite pad was washed with diethyl ether (20 mL). The crude residue obtained by evaporation of solvent was purified by silica gel column chromatography with petroleum ether/ethyl acetate (1:9) as eluent to afford the hydroxy ester **18** (0.44 g, 94% yield) as a colorless oil. R_f 0.6 (1:4 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +41.7 (*c* 2.60, $CHCl_3$); IR (neat) 3461, 2930, 2858, 1744, 1371, 1217, 1071 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.35 (dd, 1H, *J* = 5.8, 3.5 Hz), 4.1 (m, 1H), 3.88 (dd, 1H, *J* = 8.0, 3.5 Hz), 3.82 (s, 3H), 2.98 (d, 1H, *J* = 5.9 Hz), 1.55−1.42 (m, 3H), 1.40 (s, 3H), 1.37

(s, 3H), 1.31−1.23 (brm, 9H), 0.88 (t, 3H, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 109.0, 82.0, 76.6, 70.7, 52.6, 33.3, 31.7, 29.5, 29.1, 27.4, 26.7, 25.8, 22.6, 14.0; HRMS (m/z) $[M + Na]^+$ calcd for $C_{15}H_{28}O_5$, 311.1834; found, 311.1832.

Preparation of 19. To a stirred solution of **18** (0.42 g, 1.46 mmol) in dry DMF (4 mL) were added imidazole (0.3 g, 4.38 mmol) and DMAP (35 mg, 0.29 mmol). After 15 min of stirring at room temperature, TBDMSCl (0.44 g, 2.92 mmol) was introduced into the reaction mixture, which was stirred at room temperature for 6 h. The reaction mixture was then poured into water (10 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried (Na_2SO_4). Evaporation of solvent followed by silica gel column chromatography of the crude residue with petroleum ether/ethyl acetate (95:5) as eluent afforded the silyl ether **19** as a colorless oil in 94% (0.32 g) yield. R_f 0.6 (1:9 EtOAc/petroleum ether); $[\alpha]^{26}_D$ −0.39 (c 3.90, $CHCl_3$); IR (neat) 2931, 2859, 1760, 1464, 1255 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.29 (d, 1H, J = 4.7 Hz), 4.10−4.00 (m, 1H), 3.88−3.85 (m, 1H), 3.73 (s, 3H), 1.53−1.22 (m, 18H), 0.95−0.82 (m, 12H), 0.06 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 108.9, 81.6, 77.7, 73.0, 51.8, 33.8, 31.7, 29.6, 29.1, 27.5, 27.0, 26.0, 25.6, 22.6, 18.2, 14.0, −5.1, −5.2; HRMS (m/z) $[M + Na]^+$ calcd for $C_{21}H_{42}O_5Si$, 425.2699; found, 425.2696.

Preparation of 20. Diyne was synthesized following the same procedure described for the synthesis of **16.** Yield 58% (colorless oil). R_f 0.4 (1:9 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +130.5 (c 2.30, $CHCl_3$); IR (neat) 3418, 2955, 2858, 1111, 1060 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.64 (m, 4H), 7.42−7.36 (m, 6H), 5.84 (ddd, 1H, J = 16.6, 10.5, 5.3 Hz), 5.38 (d, 1H, J = 16.9 Hz), 5.13 (d, 1H, J = 10.2 Hz), 4.83 (d, 1H, J = 5.2 Hz), 4.52−4.51 (m, 1H), 4.02 (dt, 1H, J = 8.0, 4.0 Hz), 3.78 (dd, 1H, J = 3.5, 7.9 Hz), 2.57 (brs, 1H), 1.42−1.26 (m, 18 H), 1.08−1.06 (s, 9H), 0.87 (t, 3H, J = 7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.2, 135.9, 135.7, 134.8, 133.0, 132.7, 129.9, 129.6, 127.62, 127.60, 127.5, 116.1, 109.3, 82.5, 78.9, 77.3, 76.4, 71.1, 69.3, 64.9, 63.0, 33.7, 31.7, 29.5, 29.1, 27.5, 26.86, 26.80, 26.5, 25.9, 22.6, 19.3, 14.1; HRMS (m/z) $[M + Na]^+$ calcd for $C_{36}H_{48}O_4Si$, 595.3220; found, 595.3220.

Preparation of 1e. Compound **1e** was synthesized following a similar procedure described for the synthesis of **1c**. Yield 69% (white solid). R_f 0.5 (3:2 EtOAc/petroleum ether); mp 77−78 °C; $[\alpha]^{26}_D$ −31.7 (c 1.50, MeOH); IR (KBr) 3352, 2954, 2925, 2856, 1611, 1415, 1022 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 5.92 (ddd, 1H, J = 16.7, 10.1, 5.5 Hz), 5.40 (d, 1H, J = 17.0 Hz), 5.19 (d, 1H, J = 10 Hz), 4.43 (d, 1H, J = 7.3 Hz), 3.82−3.70 (m, 1H), 3.38 (brd, 1H, J = 7.5 Hz), 3.32 (brs, 1H), 1.53−1.32 (m, 12H), 0.90 (t, 3H, J = 7 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 138.1, 116.6, 81.4, 78.9, 76.6, 71.0, 70.4, 69.5, 64.6, 63.8, 34.5, 33.0, 30.7, 30.4, 26.9, 23.7, 14.4; HRMS (m/z) $[M + Na]^+$ calcd for $C_{17}H_{26}O_4$, 317.1729; found, 317.1734.

Preparation of 24. In an oven-dried two-neck 100 mL round-bottom flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed hexyltriphenylphosphonium bromide (3.37 g, 7.9 mmol). THF (10 mL) was added, and the mixture was was cooled to 0 °C. n-BuLi (3 mL, 2.6 M in hexane, 7.9 mmol) was added slowly dropwise to the reaction mixture, which was stirred for 15 min. A solution of the lactol **23** (0.5 g, 2.63 mmol) dissolved in THF (8 mL) was introduced into the reaction mixture. The resulting solution was stirred at room temperature for 16 h, cooled to 0 °C, slowly quenched with a saturated solution of citric acid (10 mL), and extracted with diethyl ether (3 × 10 mL) . The combined ethereal layers were washed with brine (10 mL) and dried over Na_2SO_4. Evaporation of the solvent followed by column chromatography of the resulting residue using petroleum ether/EtOAc (7:3) yielded **24** (0.4 g, 60%) as a colorless oil (E/Z = 3:7). R_f 0.4 (3:2 EtOAc/petroleum ether); IR (neat) 3413, 2956, 2928, 1379 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89−5.51 (m, 2H), 4.63 (m, 1H), 4.17−3.61 (m, 2H), 2.58 (brs, 2H), 2.20−2.01 (m, 3H), 1.43−1.01 (m, 14H), 0.71 (t, 3H, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.6, 124.9, 108.6, 78.4, 78.1, 69.9, 64.2, 32.2, 31.3, 28.6, 27.7, 25.2, 22.4, 14.0; HRMS (m/z) $[M + Na]^+$ calcd for $C_{14}H_{26}O_4$, 281.1729; found, 281.1722.

Preparation of 22. To a solution of **24** (0.33 g, 1.28 mmol) in 2 mL of MeOH at room temperature was added activated 10% Pd/C (60 mg). The reaction mixture was stirred for 3 h under hydrogen atmosphere (balloon) at the same temperature. After the reaction was complete (TLC), the mixture was filtered through a short pad of Celite, and the Celite pad was washed with ether (15 mL). Evaporation of solvent followed by column chromatography of the resulting residue using petroleum ether/EtOAc (7:3) yielded **22** (0.3 g, 96%) as a colorless oil. R_f 0.4 (3:2 EtOAc/petroleum ether); $[\alpha]^{26}_D$ −8.3 (c 3.20, $CHCl_3$); IR (neat) 3401, 2927, 2858, 1379 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.23−4.16 (m, 1H), 3.98−3.92 (m, 1H), 3.84−3.72 (m, 3H), 2.60−2.30 (brm, 2H), 1.82−1.62 (m, 3H), 1.58−1.49 (m, 15H), 0.88 (t, 3H, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.0, 77.9, 77.7, 69.6, 64.7, 31.8, 29.6, 29.3, 29.2, 28.0, 26.6, 25.6, 22.6, 14.0; HRMS (m/z) $[M + Na]^+$ calcd for $C_{14}H_{28}O_4$, 283.1885; found, 283.1873.

Preparation of 25. To a stirred solution of the diol **22** (0.7 g, 2.7 mmol) in toluene (15 mL) was added $(n\text{-Bu})_2SnO$ (0.67 g, 2.7 mmol), and the mixture was was refluxed using a Dean−Stark water trap for 18 h. BnBr (0.3 mL, 2.7 mmol) and TBAI (tetra n-butyl ammonium iodide) (2 g) were added to the reaction mixture and refluxed for further 2 h. The mixture was was cooled to room temperature, and most of the toluene was removed under reduced pressure. The residue thus obtained was diluted with CH_2Cl_2 (10 mL), water (5 mL) was added to it, and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Evaporation of the solvent followed by column chromatography of the resulting residue using petroleum ether/EtOAc (9:1) yielded the benzyloxy ether (0.75 g, 80%) as a colorless oil. R_f 0.6 (1:4 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +0.2 (c 2.60, $CHCl_3$); IR (neat) 3582, 3467, 2984, 2927, 2858, 1454, 1378 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.26 (m, 5H), 4.58 (s, 2H), 4.17 (ddd, 1H, J = 9.4, 5.4, 3.6 Hz), 3.95 (dd, 1H, J = 9.1, 5.1 Hz), 3.87−3.83 (m, 1H), 3.74 (dd, 1H, J = 9.5, 2.7 Hz), 3.57 (dd, 1H, J = 9.4, 6.7 Hz), 2.48 (d, 1H, J = 4.8 Hz), 1.72−1.27 (m, 18H), 0.87 (t, 3H, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 128.4, 127.7, 107.8, 78.1, 77.4, 73.4, 72.1, 68.4, 31.8, 29.6, 29.3, 29.2, 28.2, 26.5, 25.7, 22.6, 14.0; HRMS (m/z) $[M + Na]^+$ calcd for $C_{22}H_{34}O_4$, 373.2355; found, 373.2355.

To a stirred solution of the benzyloxy ether (0.42 g, 1.22 mmol) in dry DMF (5 mL) were added imidazole (0.25 g, 3.7 mmol) and DMAP (30 mg, 0.24 mmol). After 15 min of stirring at room temperature, TBDMSCl (0.37 g, 2.44 mmol) was introduced into the reaction mixture, which was stirred at room temperature for 6 h. The reaction mixture was then poured into water (10 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried (Na_2SO_4). Evaporation of solvent followed by silica gel column chromatography of the crude residue with petroleum ether/ethyl acetate (95:5) as eluent afforded the silyl ether **25** (0.51 g, 90%) as a colorless oil. R_f 0.7 (1:9 EtOAc/petroleum ether); $[\alpha]^{26}_D$ −25.1 (c 3.00, $CHCl_3$); IR (neat) 2954, 2929, 2857, 1461, 1249, 1101 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.26 (m, 5H), 4.53 (s, 2H), 4.15−4.01 (m, 2H), 3.97 (dt, 1H, J = 7.6, 1.8 Hz), 3.70 (dd, 1H, J = 10.0, 1.8 Hz), 3.52 (dd, 1H, J = 10.0, 5.9 Hz), 1.60−1.28 (m, 18 H), 0.89−0.86 (m, 12H), 0. 09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 128.2, 127.5, 127.4, 107.8, 78.0, 77.8, 73.3, 73.2, 71.0, 31.8, 29.8, 29.6, 29.2, 28.3, 26.1, 26.0, 25.9, 22.6, 18.2, 14.1, −3.6, −5.0; HRMS (m/z) $[M + Na]^+$ calcd for $C_{27}H_{48}O_4Si$, 487.3220; found, 487. 3223.

Preparation of 26. To a solution of **25** (0.5 g, 1.1 mmol) in EtOAc (6 mL) at room temperature was added activated 10% Pd/C (90 mg). The reaction mixture was stirred for 8 h under hydrogen atmosphere (balloon). After the reaction was complete (TLC), it was filtered through a short pad of Celite, and the Celite pad was washed with ether

(15 mL). Evaporation of the solvent followed by column chromatography of the resulting residue using petroleum ether/EtOAc (9:1) yielded **26** (0.38 g, 94%) as a colorless oil. R_f 0.5 (3:7 EtOAc/petroleum ether); $[\alpha]^{26}_D$ −37.3 (*c* 3.80, $CHCl_3$); IR (neat) 3488, 2954, 2930, 2858, 1464 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.15−4.05 (m, 2H), 3.81 (dt, 1H, *J* = 8.1, 3.8 Hz), 3.77−3.62 (m, 2H), 2.28 (dd, 1H, *J* = 8.7, 4.0 Hz), 1.72−1.43 (m, 3H), 1.42 (s, 3H), 1.34 (s, 3H), 1.32−1.25 (m, 9H), 0.87−0.85 (m, 12H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.1, 79.3, 77.9, 70.5, 65.4, 31.8, 29.8, 29.6, 29.2, 28.1, 26.2, 25.8, 22.6, 18.0, 14.0, −3.5, −4.7; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{20}H_{42}O_4Si$, 397.2750; found, 397.2756.

Preparation of 27. To a solution of the alcohol **26** (0.5 g, 1.35 mmol) was dissolved in DMSO (6 mL) and was cooled to 0 °C and IBX (0.76 g, 2.7 mmol) was added. The reaction mixture was then warmed to room temperature and stirred for 3 h at room temperature. After the reaction was over, the reaction mixture was cooled to 0 °C and quenched with ice-cold water (5 mL). The solids were filtered through a short pad of Celite, and the Celite pad was washed with diethyl ether (20 mL). The filtrate was extracted with diethyl ether (3 × 10 mL). Combined ethereal extracts were washed with brine (30 mL) and dried (Na_2SO_4). Evaporation of the solvent gave the crude aldehyde, which was subjected to the next reaction without further purification.

To a solution of the crude aldehyde obtained above in dry CH_2Cl_2 (5 mL) were added CBr_4 (1.79 g, 5.4 mmol) and zinc dust (0.35 g, 5.4 mmol). The reaction mixture was cooled to 0 °C, PPh_3 (1.4 g, 5.4 mmol) was added portionwise to it, and the mixture was stirred at 0 °C for further 1 h. Then it was diluted with hexane and filtered through a short pad of Celite, and the Celite pad was washed with diethyl ether (20 mL). Evaporation of the solvent and purification of the crude residue thus obtained by silica gel column chromatography using petroleum ether/EtOAc (98:2) gave **27** in 62% (0.44 g) yield. R_f 0.6 (5:95 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +3.4 (*c* 2.80, $CHCl_3$); IR (neat) 2955, 2929, 2858, 1253, 1070 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.37 (d, 1H, *J* = 8.8 Hz), 4.35 (t, 1H, *J* = 8.6 Hz) 4.16−4.11 (m, 1H), 3.88 (dd, 1H, *J* = 8.0, 5.7 Hz), 1.66−1.27 (m, 18 H), 0.89−0.86 (m, 12H), 0.12 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 107.9, 91.6, 79.4, 77.8, 71.9, 31.8, 29.6, 29.5, 29.2, 28.0, 26.9, 25.8, 25.4, 22.6, 17.9, 14.1, −3.8, −4.8; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{21}H_{40}Br_2O_3Si$, 551.1098; found, 551.1124.

Preparation of 28. To a dissolved solution of **27** (0.32 g, 0.6 mmol) in dry THF (8 mL) was added *n*-BuLi (0.7 mL, 1.8 mmol, 2.6 M in hexane) slowly at −78 °C and stirred at the same temperature for 30 min. The reaction mixture was then warmed to 0 °C, stirred 0.5 h at 0 °C and was allowed to come to room temperature. Progress of the reaction was monitored by TLC and after 0.5 h at room temperature it was cooled to 0 °C and was cautiously quenched with water (5 mL). It was extracted with diethyl ether (3 × 10 mL) and ethereal extracts were washed with brine (10 mL) and dried (Na_2SO_4). Evaporation of the solvent and purification of the crude residue by silica gel column chromatography with petroleum ether/ethyl acetate (98:2) as eluent afforded the alkyne **28** in 52% (115 mg) yield as a colorless oil. R_f 0.5 (5:95 EtOAc/petroleum ether); $[\alpha]^{26}_D$ −22.9 (*c* 3.70, $CHCl_3$); IR (neat) 3312, 2955, 2930, 2858, 1464, 1253 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.42 (dd, 1H, *J* = 7.7, 2.0 Hz), 4.14 (ddd, 1H, *J* = 10.0, 5.7, 3.0 Hz), 4.01 (dd, 1H, *J* = 7.7, 5.6 Hz), 2.49 (d, 1H, *J* = 2.1 Hz), 1.71−1.50 (m, 3H), 1.46 (s, 3H), 1.36 (s, 3H),1.35−1.22 (m, 9H), 0.89−0.86 (m, 12H), 0.20 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.1, 83.6, 79.9, 77.9, 76.7, 74.2, 62.3, 31.8, 29.6, 29.3, 29.2, 28.1, 26.8, 25.8, 25.6, 22.6, 18.0, 14.1, −3.9, −4.8; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{21}H_{40}O_3Si$, 391.2644; found, 391.2645.

Compound 29. To a precooled (0 °C) solution of the silyl ether **28** (0.15 g, 0.43 mmol) in THF (4 mL) was added TBAF (0.8 mL, 0.8 mmol, 1 M in THF), and the mixture was stirred at room temperature for 1 h, quenched with water (5 mL), and extracted with diethyl ether (3 × 10 mL). Combined organic layers were washed with brine and dried over Na_2SO_4. Evaporation of the solvent and purification of the resultant residue by silica gel column chromatography with petroleum ether/ethyl acetate (9:1) gave the alcohol **29** (0.1 g, 93% yield) as a colorless oil. R_f 0.6 (1:4 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +37.4 (*c* 2.20, $CHCl_3$); IR (neat) 3431, 3311, 2953, 2927, 2858, 1376, 1220, 1052 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.36 (dt, 1H, *J* = 7.1, 1.9 Hz), 4.20 (dt, 1H, *J* = 8.8, 5.8 Hz), 4.09 (t, 1H, *J* = 5.8 Hz), 2.54 (d, 1H, *J* = 2.0 Hz), 2.31 (brd, 1H, *J* = 6.7 Hz), 1.76−1.66 (m, 3H), 1.57−1.51 (m, 3H), 1.37 (s, 3H), 1.35−1.20 (m, 9H), 0.87 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.4, 89.7, 79.5, 77.3, 74.8, 62.2, 31.7, 29.5, 29.1, 28.8, 27.4, 26.9, 25.3, 22.6, 14.0; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{15}H_{26}O_3$, 277.1780; found, 277.1770.

Preparation of 21. To a solution of the alkyne **29** (98 mg, 0.39 mmol) in dry acetone (6 mL) were added NBS (139 mg, 0.78 mmol) and $AgNO_3$ (7 mg, 0.039 mmol), and the mixture was stirred for 1 h at room temperature and diluted with hexane. The mixture was filtered through a pad of Celite, and the Celite pad was washed with diethyl ether (10 mL). Residue obtained after evaporation of the solvent was further purified by silica gel column chromatography with petroleum ether/ethyl acetate (9:1) as eluent to afford **21** as a colorless oil in (125 mg) 98% yield. R_f 0.6 (1:4 EtOAc/petroleum ether); $[\alpha]^{26}_D$ +46.5 (*c* 1.80, $CHCl_3$); IR (neat) 3417, 2952, 2926, 2857, 1379, 1219, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.40−4.30 (brm, 1H), 4.19 (dt, 1H, *J* = 9.1, 6.0 Hz), 4.08 (t, 1H, *J* = 5.8 Hz), 2.56−2.50 (brs, 1H), 1.76−1.63 (m, 2H), 1.56−1.50 (m, 4H), 1.36−1.26 (m, 12H), 0.87 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.5, 79.7, 78.9, 77.2, 63.3, 46.9, 31.7, 29.5, 29.1, 28.7, 27.3, 26.9, 25.3, 22.6, 14.0; HRMS (*m*/*z*) $[M + Na]^+$ calcd for $C_{15}H_{25}BrO_3$, 355.0885; found, 355. 0872.

■ ASSOCIATED CONTENT

Supporting Information. General experimental procedures and spectroscopic data for the compounds and copies of ^1H NMR and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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